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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,112	PETERSDORF ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No: _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Claims 12-20 are withdrawn.

Claims 1-11 are examined on the merits.

Election/Restrictions

1. Applicant's election with traverse of the invention of Group I (microarray products) in the reply filed on 08/30/2006 is acknowledged. The traversal is on the ground(s) that a search and review of the full scope of the invention as claimed would not be a serious burden. This is not found persuasive because the application in a 371 of a PCT and as such the restriction of claims follows the Lack of Unity practice, wherein the lack of a special technical feature among the different groups has been determined, whereas search burden is a criteria for the restriction of claims according to US Restriction Practice. The examiner maintains that the different groups lack a special technical feature, and the response does not traverse this finding. Furthermore a search of the product (a microarray) would not be expected to be coextensive with a search of the particular methods for creating the array.

The requirement is still deemed proper and is therefore made FINAL.

Applicant has further traversed the requirement for the election of oligonucleotide probes from a particular HLA-Class I locus species selected from the group consisting of HLA-A, HLA-B, and HLA-C. This requirement is WITHDRAWN.

Claims 12-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/30/2006.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement; see for example page 2 lines 7-9. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112 2nd - Indefiniteness

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are unclear over recitation of the phrase 'of known polymorphisms', as recited in claims 1-3, in reference to a percentage of HLA Class I polymorphisms represented by a plurality of probes. While the specification provides that 'known

polymorphisms are those that have appeared in the literature or are available from a searchable database of sequences' (page 15 lines 24-26), it is unclear if applicant intends to claim a set of polymorphisms known at a particular time, or available from a particular public database. And because, for example, the polymorphisms that 'have appeared in the literature' is a constantly changing set of nucleic acid sequences, the metes and bounds of the microarray encompassed by the claim are not clearly defined.

Claims 1-11 are unclear over recitation of the term 'represent' in regard to the relationship between probes on a solid support and polymorphisms in the HLA Class I locus. It is unclear what relationship between probes and polymorphisms is encompassed by this language; for example, does applicant intend some particular level of complementarity between the required probe and a polymorphic form of an HLA Class I locus nucleic acid sequence.

Claim 5 is unclear over recitation of the phrase 'has 20 nucleic acids' in reference to a plurality of HLA Class I oligonucleotide probes, where likely 'has 20 nucleotides' is intended. Because the term 'nucleic acid' is typically used in reference to a single oligonucleotide, it is unclear if applicant intends that the claimed array specifically comprises only 20 oligonucleotides that in some way represent at least 80% of known polymorphisms in the HLA Class I locus.

Claims 6, 7, and 8 are unclear over recitation of the phrase 'said HLA Class I oligonucleotide probe' in each of claims 6, 7, and 8. The claims are unclear because, for example, Claim 6 is dependent upon claims 1 and 4, however the base claims recite only a plurality of probes, thus it is unclear if applicant intends an array comprising only

one particular probe selected from HLA-A, B and C probes. It is further unclear how a single probe would represent at least 80% of known polymorphisms, as required by the base claim 1.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (1995, US Patent 5,474,796).

Brennan teaches a microarray that contains 10-mer polynucleotides spotted at discrete locations such that the total array represents every possible permutation of 10-mer oligonucleotide (col. 9, lns. 48-55). The array of Brennan comprises every 10-mer nucleic acid, thus it would inherently comprise a plurality of probes sufficient to represent at least 80%, 90%, and 98% of known polymorphisms in the HLA Class I locus, as required by claims 1, 2, and 3, respectively.

Claim Rejections - 35 USC § 103

7. In the rejection of claims under 35 USC 103, the breadth of the claims is noted. The claimed array does not specifically require any particular probes of specific nucleic acid sequences. The claimed array requires only nucleic acid probes sufficient to represent a particular percentage of known polymorphisms in the HLA Class I locus, where the specification defines a known polymorphism as one that has appeared in the literature or available from a searchable database (page 15 of the instant specification).

The claims are thus broadly drawn to an array requiring only probes sufficient to analyze a particular percentage of HLA polymorphisms.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bettinotti et al (1997) in view of Sapolsky et al (1997, EP 0 785 280 A2).

Bettinotti et al teaches the sequence analysis and typing of HLA-A, B, and C genes from samples of genomic DNA.

Regarding the limitations of claims 1-3, the reference teaches a database of the sequence of all known HLA-A, B, and C alleles (p.425 – Abstract; p.427, right col., lns.4-12). Thus the database of all known alleles comprises sequence information for at leasts 80%, 90%, and 98% of known polymorphisms in the HLA Class I locus, relevant to claims 1, 2, and 3, respectively.

Regarding the limitations of claims 6-8, the database of Bettinotti et al, which comprise all known HLA-A, B, and C alleles, because of its comprehensive nature, has sequence information pertaining to alleles of HLA-A, B, and C (relevant to claim 6). Relevant to claims 7 and 8, the reference specifically teaches using the database in a comparison of the sequences of exons 2 and 3 (Fig 1; p.427, right col., lns.4-12) of HLA-A, B, and C.

Bettinotti et al does not teach a microarray of oligonucleotides comprising a plurality of HLA Class I oligonucleotide probes.

Sapolsky et al teach a microarray of oligonucleotides for the detection of polymorphisms. Relevant to claims 1-3, the reference teaches that an oligonucleotide array may comprise particular oligonucleotide probes complementary to particular polymorphic forms of segments of a nucleic acid sequence (e.g.: p.4. lns.23-29) and probes may encompass one or more polymorphic positions (e.g.: p.4 lns.47-48; Fig 3).

Regarding claims 4 and 5, Sapolsky et al specifically teach that an array for the analysis of polymorphic positions within a given sequence may be comprised of probes of 20 nucleotides in length (e.g.: Fig. 3; p.8, Example 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created an array of oligonucleotides probes, as taught by Sapolsky et al, using the sequence information of all of the known alleles of HLA-A, B, and C from a database as taught by Bettinotti et al. One would have been motivated to create such an array based on the assertion of Sapolsky et al that methods using such an array allow for the rapid, automatable analysis of polymorphisms (p.1 – Abstract), and the teaching of Bettinotti et al that molecular testing for HLA typing by sequence analysis allows for higher resolution (p.425, left col., last paragraph).

10. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bettinotti et al (1997) in view of Sapolsky et al (1997, EP 0 785 280 A2) and further in view of McGall et al (1995 US Patent 5,412,087)

The teachings of Bettinotti et al in view of Sapolsky et al are applied to claim 9 as they were previously applied to claims 1-8.

Bettinotti et al in view of Sapolsky et al do not specifically teach a microarray wherein the solid support is a glass slide.

McGall et al teaches spatially-addressable immobilization of oligonucleotides to create arrays using photolithographic techniques (col.3 lns.35-45). McGall et al specifically teaches arrays wherein the solid support is a glass slide (e.g. Example 1, col.12)

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the glass slide support of McGall et al for the HLA probe array of Bettinotti et al in view of Sapolsky et al. One would have been motivated to do so based on the teachings of McGall et al that such a support can be used for the immobilization of oligonucleotide probes and successful analysis of nucleic acid sequences by hybridization (e.g. Examples 3-6).

11. Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bettinotti et al (1997) in view of Sapolsky et al (1997, EP 0 785 280 A2) and further in view of Lockhart et al (1996 US Patent 5,556,752)

The teachings of Bettinotti et al in view of Sapolsky et al are applied to claims 10 and 11 as they were previously applied to claims 1-8.

Bettinotti et al in view of Sapolsky et al do not specifically teach a microarray wherein the surface density is about 250 to about 450 angstom^2/molecule (relevant to claim 10) or about 325 to about 375 angstom^2/molecule (relevant to claim 11).

Lockhart et al teaches microarrays of oligonucleotide probes generated by photolithographic methods (col.12). The reference specifically teaches that oligonucleotides on the array are approximately 100 angstroms apart (col. 22, lns.54-56), which is a surface density of about 250 to about 450 angstom^2/molecule (relevant to claim 10) and about 325 to about 375 angstom^2/molecule (relevant to claim 11).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made the microarray of Bettinotti et al in view of Sapolsky et al with a surface density as taught by Lockhart et al. One would have been motivated to do so based on the assertion of Lockhart et al that such a density allows for the immobilized probes to participate in the formation of a duplex (col. 21, lns.53-55),

and the teaching of Sapolsky et al that immobilized probes are useful for the analysis of polymorphisms by a process of hybridization (Example 2).

Conclusion

12. No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen Kapushoc
Art Unit 1634

DIANA JOHANNSEN
PRIMARY EXAMINER